

Amendments to the Specification:

On page 1, please amend the title as follows:

~~Method of Degrading Transcriptional Factors of Saccharometabolism-Associated Gene~~
Degradation, Method of for Inhibiting the Degradation, and Degradation Inhibitor Agent for
Inhibiting Degradation, for Transcription Factors of Glucose Metabolism-Related Genes

On page 1, after the title, please insert the following paragraph:

This application is a National Stage Application of PCT/JP2003/011046, filed August 29, 2003.

Please amend paragraph number [019] as follows:

[019] That is, one aspect of the present invention relates to a method for degrading a transcription factor of a glucose metabolism-related gene, wherein the method comprises making calpain coexist with the transcription factor of the glucose metabolism-related gene in the presence of calcium. Another way of describing this aspect of the invention is that the method for degrading a transcription factor of a glucose metabolism-related gene comprises providing a condition wherein calpain and the transcription factor can interact with each other in the presence of calcium.

Please amend paragraph number [020] as follows:

[020] Another aspect of the present invention relates to a method for degrading a transcription factor of a glucose metabolism-related gene, wherein the method comprises changing the degree of degradation of the transcription factor of the glucose metabolism-related gene by changing the calcium concentration.

Please amend paragraph number [071] as follows:

[071] Another aspect of the present invention relates to a method for regulating production of a gene product of a glucose metabolism-related gene, wherein the method comprises changing a degree of the degradation of a transcription factor of the glucose metabolism-related gene by-a changing the calcium concentration.

Please amend paragraph number [072] as follows:

[072] A further aspect of the present invention relates to a method for regulating production of a gene product of a glucose metabolism-related gene, wherein the method comprises changing the degree of degradation of at least one member selected from the group consisting of hepatocyte nuclear factor 4 α , hepatocyte nuclear factor 1 α and insulin promoter factor 1 by-a changing the calcium concentration.

Please amend paragraph number [0163] as follows:

[0163] An agent for inhibiting the degradation of a transcription factor of a glucose metabolism-related gene, according to one aspect of the present invention, contains as an active ingredient, an effective dose of at least one member selected from the group consisting of the following: a substance inhibiting the binding of the transcription factor to calpain; a substance inhibiting the cleavage of the transcription factor caused by calpain; and a substance inhibiting calpain activity. The agent for inhibiting the degradation of a transcription factor may be an inhibitory agent containing, as an active ingredient, an effective dose of at least one member selected from the group consisting of the following: a substance inhibiting the binding of one kind of transcription factor to calpain; a substance inhibiting the cleavage of the transcription

factor by calpain; and a substance inhibiting calpain activity. Further, the inhibitory agent may contain a combination of plural kinds of inhibitory substances for each transcription factor. More specifically, for example, the inhibitory agent preferably contains as an active ingredient, an effective dose of at least one member selected from the group consisting of the following: a substance inhibiting the binding of calpain to HNF-4 α , HNF-1 α , or ~~IPE-1~~~~IPF-1~~ α ; a substance inhibiting the cleavage of HNF-4 α , HNF-1 α , or ~~IPE-1~~~~IPF-1~~ α caused by calpain; and a substance inhibiting calpain activity.

Please amend paragraph number [0164] as follows:

[0164] A method for inhibiting the degradation of a transcription factor of a glucose metabolism-related gene, according to one aspect of the present invention, comprises using at least one member selected from the group consisting of the following: a substance inhibiting the binding of calpain to the transcription factor; a substance inhibiting the cleavage of the transcription factor by calpain; and a substance inhibiting calpain activity. In this case, the method for inhibiting the degradation of a transcription factor may comprise using at least one member selected from the group consisting of the following: a substance inhibiting the binding of calpain to one kind of transcription factor; a substance inhibiting the cleavage of the transcription factor by calpain; and a substance inhibiting calpain activity, as well as using plural kinds of such inhibitory substances for each transcription factor in combination. More specifically, for example, the method preferably comprises using at least one member selected from the group consisting of the following: a substance inhibiting the binding of calpain to HNF-4 α , HNF-1 α , or ~~IPE-1~~~~IPF-1~~ α ; a substance inhibiting the cleavage of HNF-4 α , HNF-1 α , or ~~IPE-1~~~~IPF-1~~ α by calpain; and a substance inhibiting calpain activity.

Please amend paragraph number [0167] as follows:

[0167] Another aspect of the method for regulating production of a gene product of a glucose metabolism-related gene can be a method that comprises regulating production of a gene product of a glucose metabolism-related gene by modulating the calcium concentration to regulate the degradation of a transcription factor involved in expression of the gene-factor to a desired degree. By providing a high calcium concentration to activate calpain, a transcription factor involved in expression of a glucose metabolism-related gene can be degraded, and thereby production of the gene product of a gene on which the transcription factor acts can be lowered. Further, by providing a low calcium concentration to attenuate the enzyme activity of calpain, the degradation of the transcription factor can be inhibited, and thereby production of the gene product can be enhanced.